

Statistics, Symmetry & Synthesis

- “... *thermodynamics ... is the only physical theory of ... which I am convinced, ... its basic concepts will never be overthrown.*” – Einstein
- “C'est la dissymétrie qui crée le phénomène” – P Curie
- La chimie crée son objet. Cette faculté créatrice, semblable à celle de l'art lui-même, la distingue essentiellement des sciences naturelles et historiques – M Berthelot

Molecular Design & Synthesis

- Chemistry - Study of matter and its transformations
Architecture - Art and science of building
Sculpture - Art of forming matter
- La chimie crée son objet. Cette faculté créatrice, semblable à celle de l'art lui-même, la distingue essentiellement des sciences naturelles et historiques” – Berthelot 1860





Problem (re)Solving

Problems to find - demonstration based
 “Can we find a drug to bind to this receptor?”

Problems to prove - deduction based.

“How or why does this interact?”

Problems to create -Humanist conflicts

man/nature, man/machine,
 man/society, man/himself



Models and Myths

Scientific Method and Chance

➤ Science stands on *conjecture* and critical attempts at *refutation*

➤ Refutation can be countered by *amendment* or *revolution*



Popper



Kuhn



Feyerabend



Pasteur

➤ ... only principle that does not inhibit progress is: *anything goes*

➤ Chance favors the “prepared” mind

Truth, Reality, and Modeling

➤ Truth is Chaos

➤ Reality is the Human Experience of Chaos
(Empiricism and Perception)

➤ You want the truth...You can't handle the truth
-Jack Nickolson to Tom Cruise

➤ Modeling is the opiate of the masses
(human's way to cope with chaos)
-essentially Karl Marx

Empiricism and Rationality



- ◆ Experience is the name everyone gives to his mistakes - Oscar Wilde
- ◆ Our whole problem is to make mistakes as fast as possible - J.A. Wheeler



Objects and Models

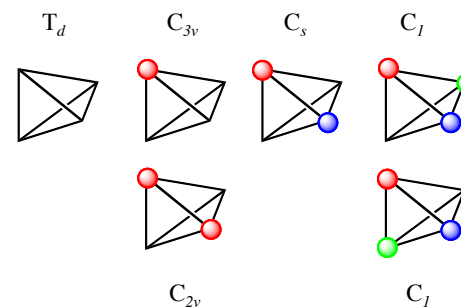


Molecular Models

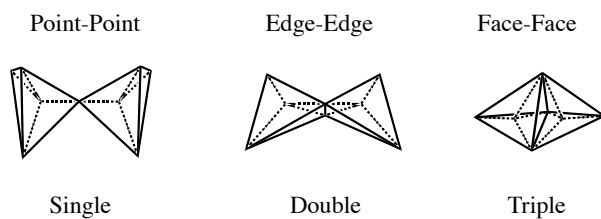
- visualizing the microscopic world of atoms
- van 't Hoff's initial cardboard set



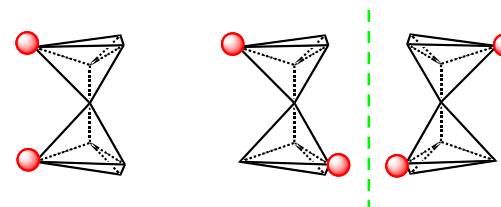
Asymmetry and Isomerism



Tetrahedral Valency and Multiple Bonds



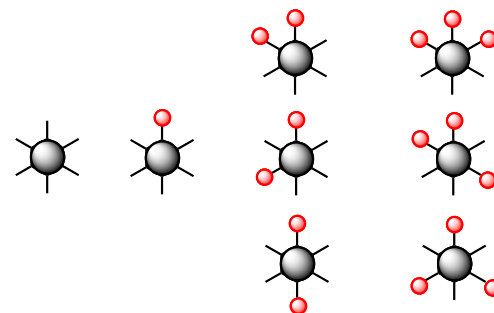
Paterno and Free Rotation



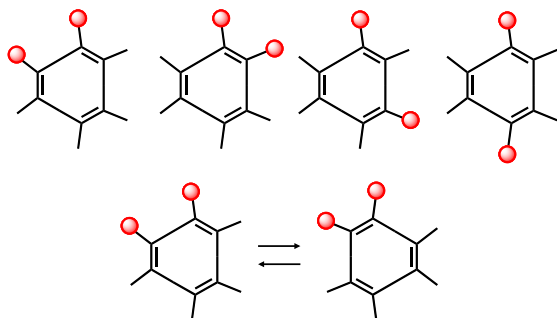
A. Kekulé (1829-1896)



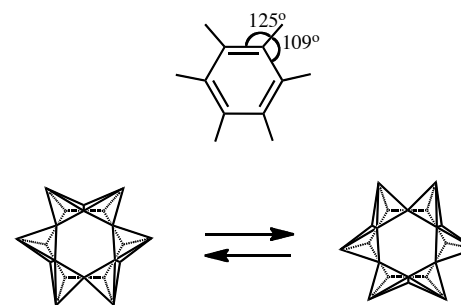
Koerner's Isomer Counting Criteria



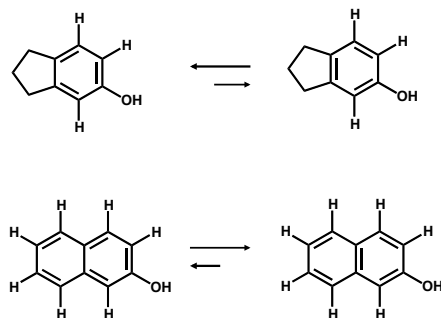
Oscillation Hypothesis



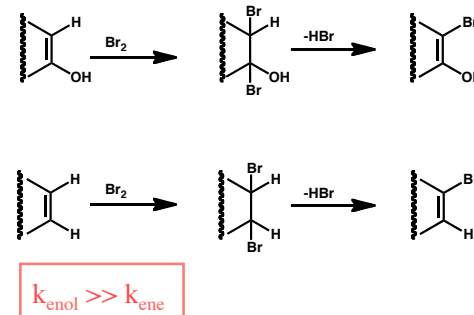
Tetrahedral Carbon Applied to Benzene



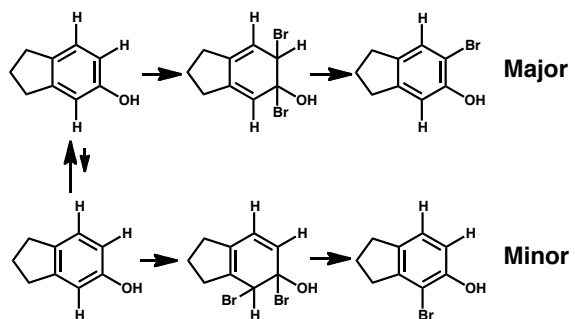
Mills-Nixon Proposal



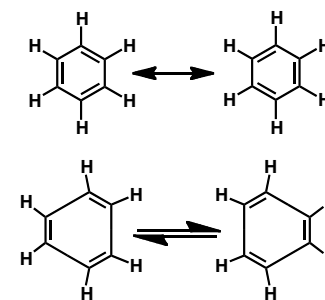
Bromination of Enols vs. Alkenes



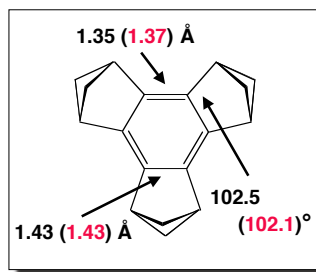
Bromination Experiments on Indanol



Mesomerism and Resonance

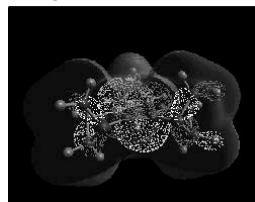


Modern View of Strain Effects on Benzene

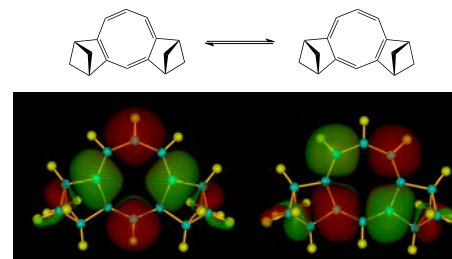


Tribicyclo[2.1.1]hexabenzene

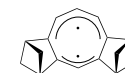
Can one find
a) an explanation for the
observed reactivity?
b) a system that acts like
a single Kekulé tautomer?



Planar Delocalized Cyclooctatetraene



JACS, 2001, 123, 1755.



Singlet diradical C_{2v}



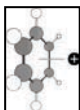
Belief begets bias or Feyerabend's revenge

Blinded by Faith - Mathew 7:7

- Ask, and it shall be given you; seek, and ye shall find.
- Searching for **effects** can always leads to some affirmative perspective.
- In a plethora of data there will always be a surfeit of folly.

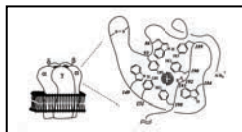
Cation- π Interaction

- Gas Phase Studies
- Calculations



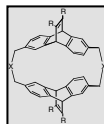
Kebarle JPC 1981, 85, 1814
JACS 1984, 106, 3959
Dougherty JACS

- Biological Systems



N. Unwin, J. Mol. Bio. 229, 1101
Dougherty Nature 2009, online

- Host Guest Studies



Dougherty
JACS 1988, 110, 6825.

Review: Dougherty, Chem. Rev. **1997**, 97, 1303
JOC **2008**, 73, 3667

I. Benzene K⁺ in Gas Phase

EM Arnett in J Chem Ed 1985 (Cited 37 times source ISI)

Water, like the other simple hydrides, is a relatively weak acid and base in the gas phase compared to its substituted derivatives whose conjugate acid or base ions can be stabilized by polarization of organic groups. Correspondingly, single H₂O molecules solvate ions feebly compared to larger and more polarizable molecules whose bulk liquids are grossly inferior to bulk water as a medium for ions.

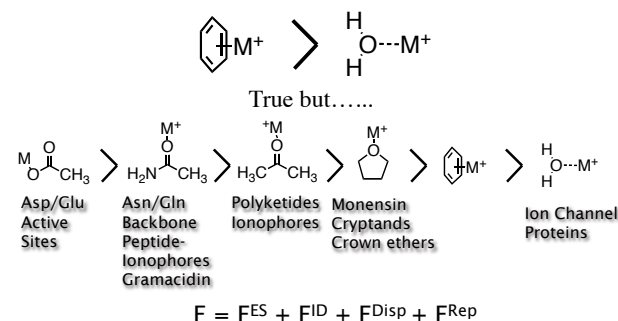
Thus single molecules of methanol and acetonitrile outclass single H₂O molecules for stabilizing gas phase halide ions (**2e**) and even benzene is superior to H₂O for complexing potassium ions (52)! As more water molecules are added to develop a hydrogen bonded cluster, water rapidly demonstrates its superior solvation properties

II. Benzene K⁺ in Gas Phase

D. Dougherty in Chem. Rev. 1997 (cited 1538 times, source ISI)

Still, without some kind of external reference, it is difficult to know to what extent cation- π interactions might be important in a condensed phase. Fortunately, the pioneering work of Kebarle² provided the perfect reference compounds water. All would agree that the interaction of an ion such as K⁺ with water should be strong in the gas phase, and it is. The K⁺ - water interaction energy is 18 kcal/mol. But, the K⁺ - benzene interaction energy is 19 kcal/mol! In fact, throughout a series of ion-molecule complexes with K⁺ binding from one to four molecules of benzene or water, the benzene complexes are stronger.²

Benzene vs Water



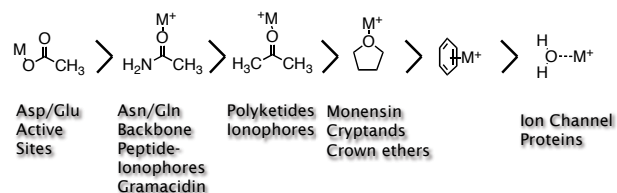
J. Sunner, K. Nishizawa, P. Kebarle *J. Phys. Chem.*, **1981**, 85, 1814-1820

J. Sunner, P. Kebarle *J. Am. Chem. Soc.*, **1984**, 106, 6135-6139

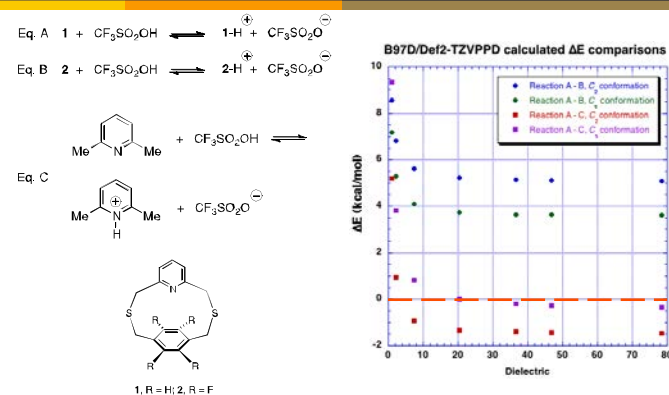
Benzene vs Water

Sunner, Jan; Nishizawa, Kazushige; Kebarle, Paul. **Ion-solvent molecule interactions in the gas phase. The potassium ion and benzene.** *Journal of Physical Chemistry* (1981), 85(13), 1814-20. (Cited 187 times by Sci Finder; 235 ISI)

Sunner, Jan; Kebarle, Paul. **Ion-solvent molecule interactions in the gas phase. The potassium ion and dimethyl sulfoxide, DMA, DMF, and acetone.** *Journal of the American Chemical Society* (1984), 106(21), 6135-9. (Cited 35 times by Sci Finder; 55 ISI)

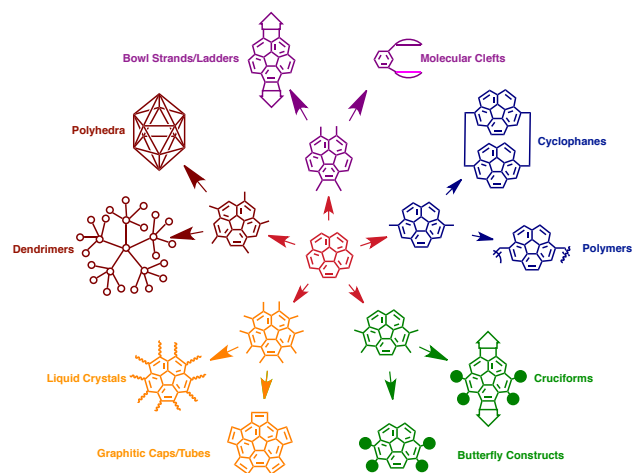
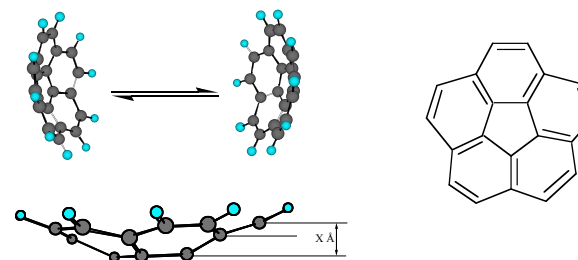


Solvation vs cation- π effect

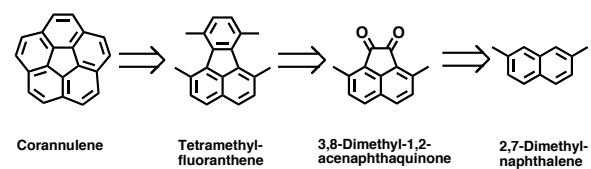


Sculpting a personal dream

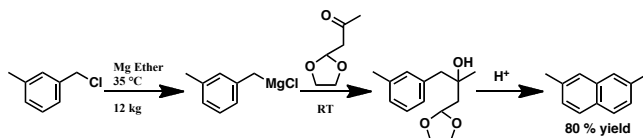
Corannulene as Aromatic Bowl



Retrosynthesis of Corannulene

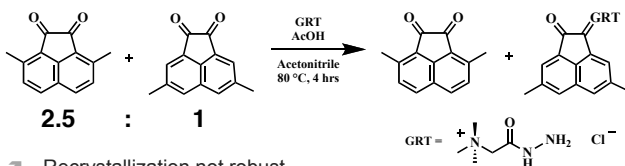


Dimethylnaphthalene



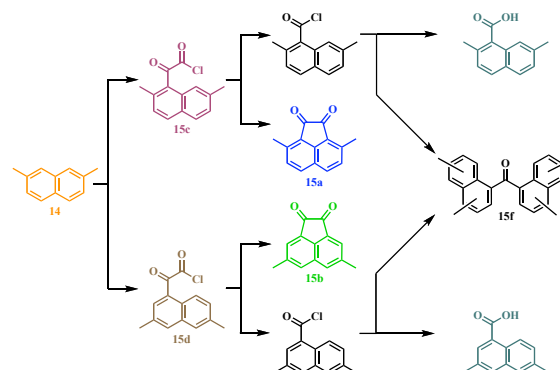
- Chloro Grignard due to solubility
- Ether due to side product formation
- Heat profile stable and safe
- Telescoping of addition/cyclization
- Volume yield ca. 10%
- Technical purity OK

Girard's Reagent

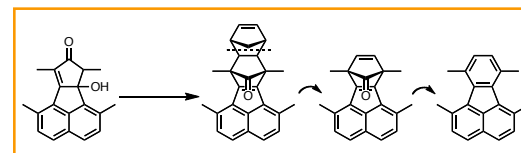
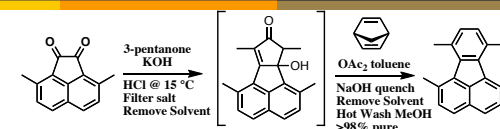


- Recrystallization not robust
- Chromatography not applicable
- In situ derivatization allows aqueous extraction of side product
- Product isolated by filtration (98% purity)
- Side product recovered after hydrolysis. (90 % purity)

Acylation Chemistry



Tetramethylfluoranthene

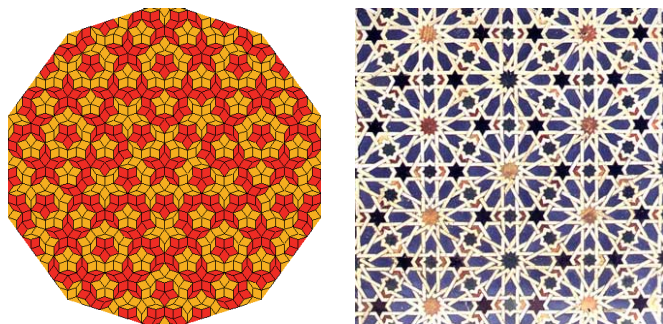


Simplify work up ; Increase volume yield

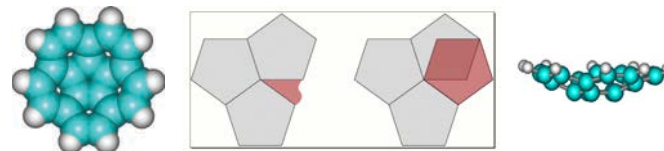
Telescope condensation/cycloaromatization

Develop column free purification

Distribution of Tiles in the Plane

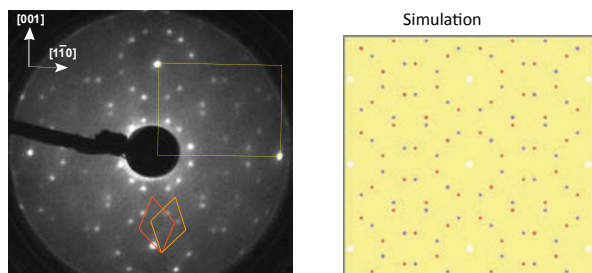


Tiling Pentagons



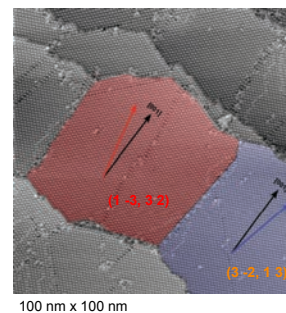
- 5-fold symmetry incommensurate with lattice.
- Distortions allow multiple arrangements (polymorphism in 2-D)
- Symmetry breaking and 2-D conglomerates

Enantiomorphous Lattices



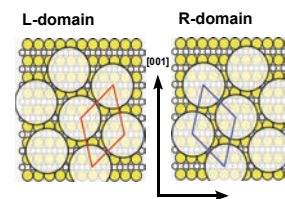
Adsorption induced organisational chirality

Coexistence of Mirror Domains



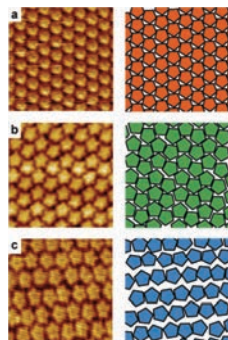
Structure models:

- close-packed quasi-hexagonal overlayer
- three different NN-distances of 10.5, 10.8 and 11.1 Å

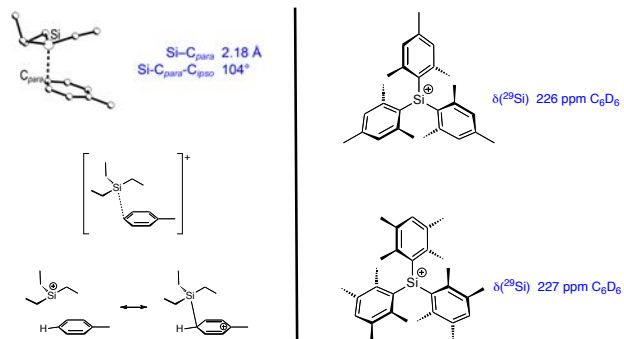


Analog Solutions

- Tiling the plane
- Optimal molecular packing
- Efficiency of plastic part production
- Percolation theory with metallic objects

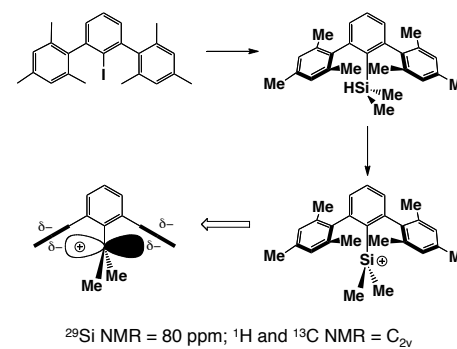


Two influential experiments

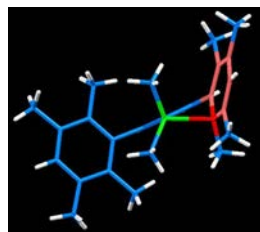
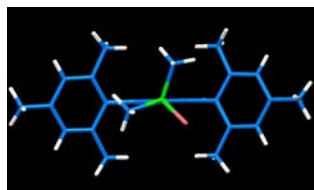
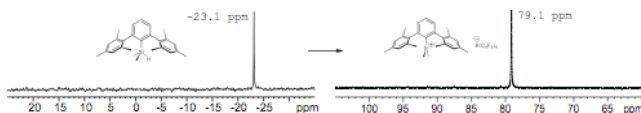


Chance and Preparedness

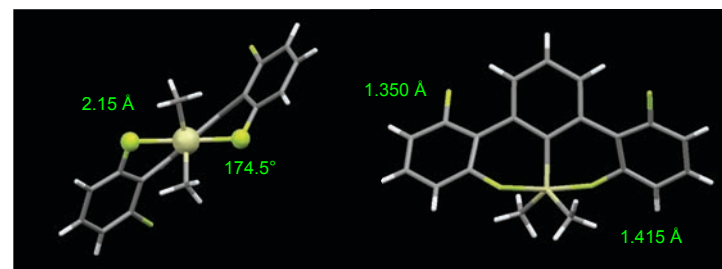
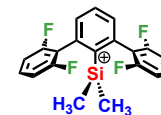
Silicon Cations - Synthesis



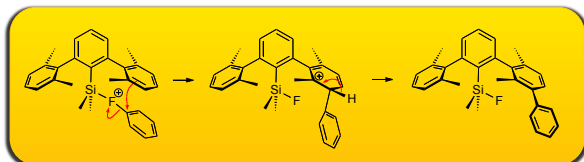
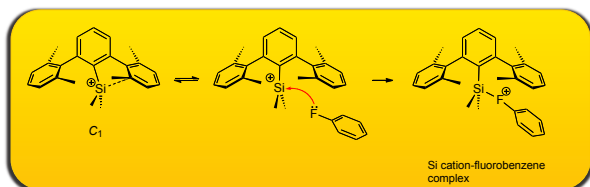
Silyl Cations - Crystal vs Solution Structure



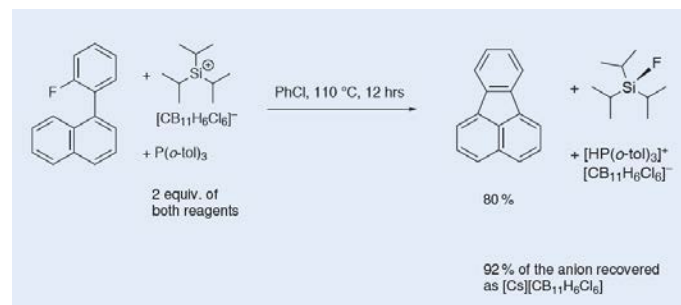
Silonium or Fluorenium?



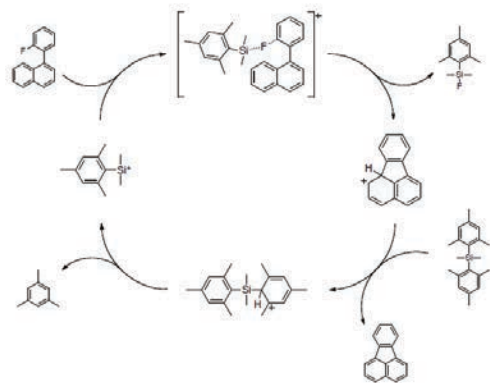
Fluorobenzene Activation



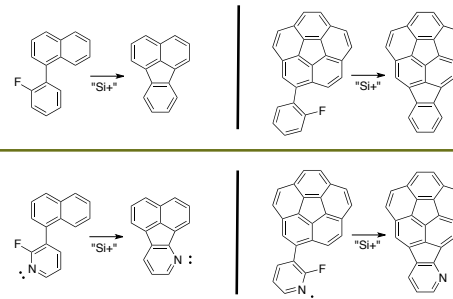
Friedel-Crafts Arylations



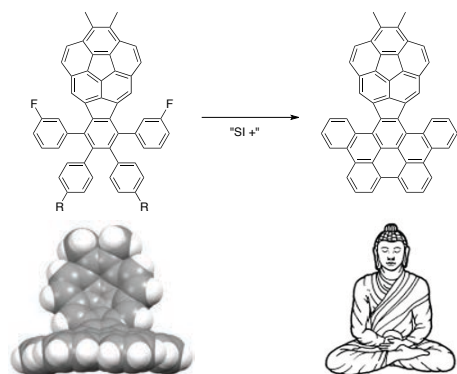
Proposed Mechanism



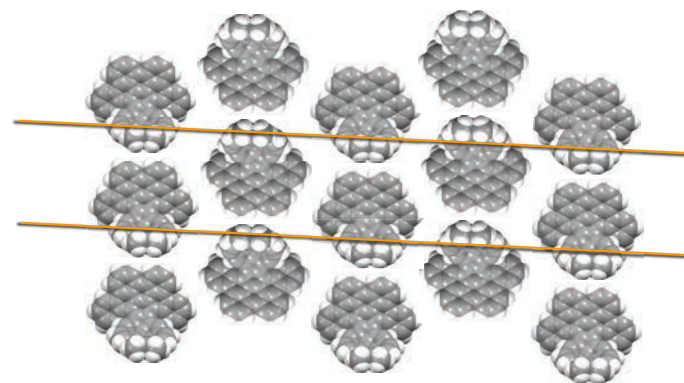
Indeno and Azaindeno



Sitting Buddha - Lotus



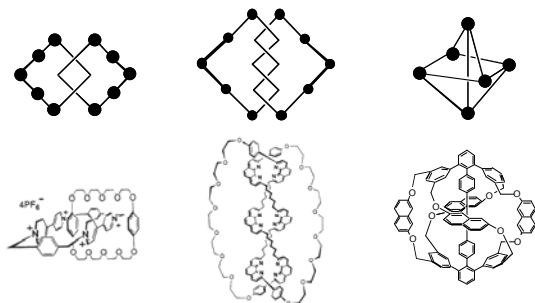
Graphene Furrows (Hypothesis)



Network Complexity, “Emergence” and Systemic Instability

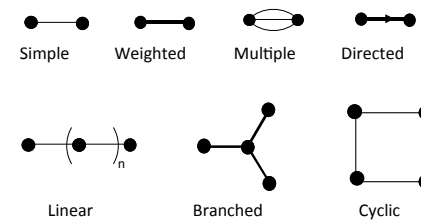
Graphs to Topological Isomers

➤ Complex molecular design from graphs

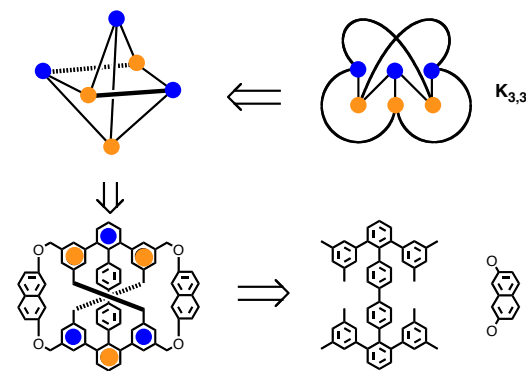


Graph Theory

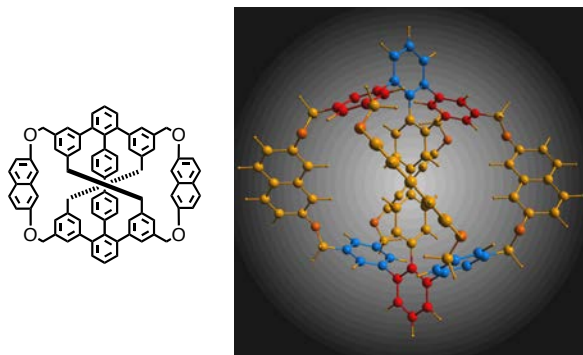
➤ Graph is a set of points and their connections.



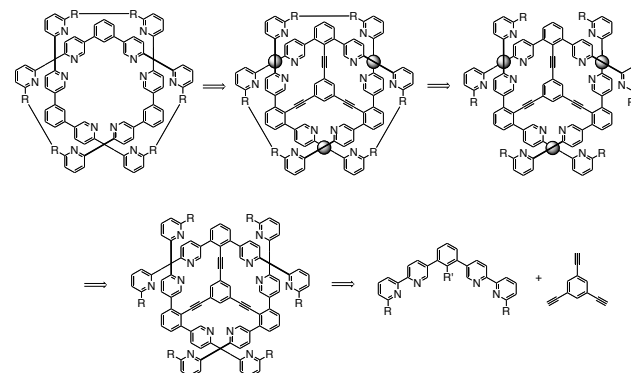
Loschmidt Replacement



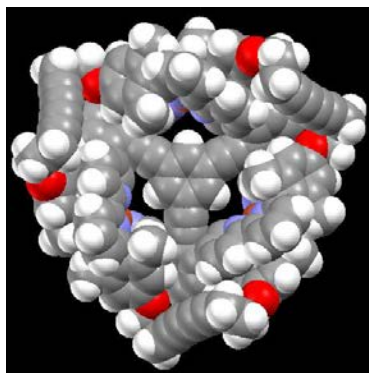
Kuratowski Cyclophane



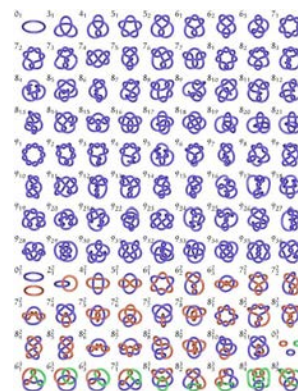
Trefoil Knot Retrosynthesis



Tying the knot



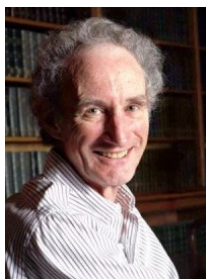
Complex Knots and Lacings



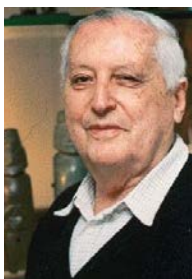
Lorenz, May and Prigogine



Meteorology



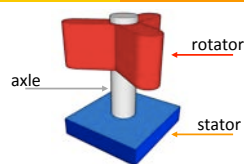
Ecology



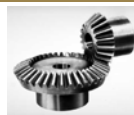
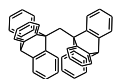
Chemistry

Machines and Devices

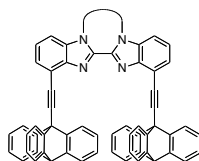
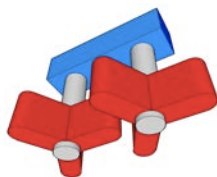
Defining a Molecular Gear



dynamic gearing



Bevel Gears

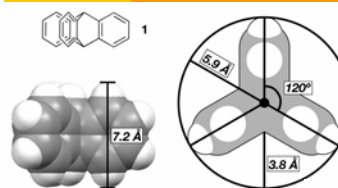


Spur Gears

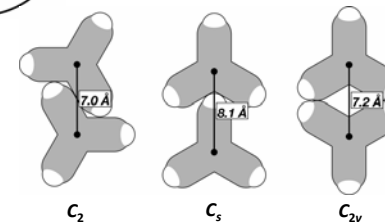
Photographs of gears courtesy of Emerson Power Transmission Corporation (<http://www.emerson-ept.com>)



Triptycenes in Parallel

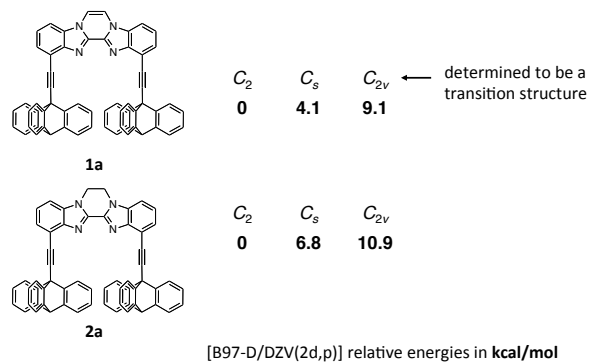


For geared rotation to be preferred over gear slippage, van der Waals interactions must stabilize the C_2 and C_s conformations and/or destabilize the C_{2v} conformation.



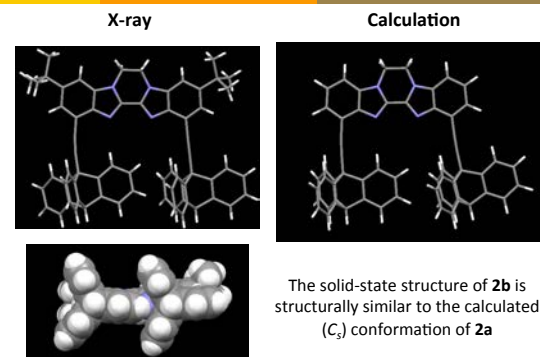
Frantz, D. K.... *Chimia*, **2009**, 63, 201.

Computational Results



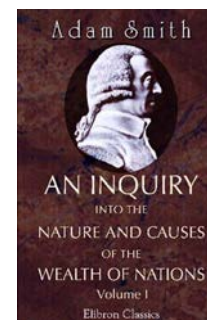
K. K. Baldridge, 2009

Structural Parallels



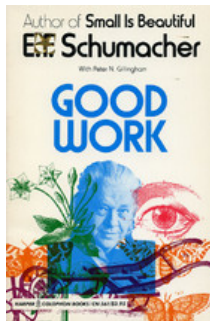
Intellectual Sustainability

Idolatry of Economic Productivity



- Labor Saving but dehumanizing
- Automation better for humanity?
- Division of Labor simplifies the scope of daily tasks and ultimately renders the worker incapable of even simple judgments regarding civic life.
- No social order without civic education.

Pride in Work



- Labor saving devices are not the panacea they are made out to be.
- Humans need physical and mental labor that keeps their minds and bodies healthy.
- Leisure is not a substitute for creative labor.
- Ethical commitment to Humanity

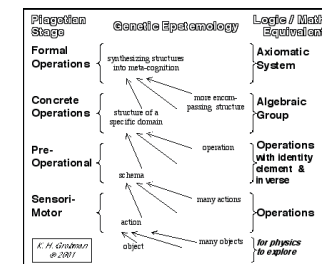
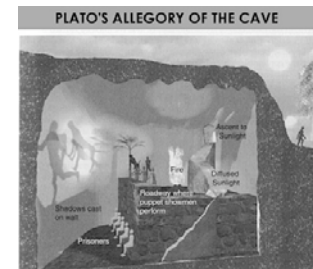
Education and Democracy

Tyranny, Knowledge and Democracy

- The will of the majority alone cannot protect the interest of the minority.
- Right to know, bears a responsibility to understand
- Gap in communal civic education means a deficiency in Democracy
- Liberal Education including precepts of scientific thought predicate modern democratic governance.

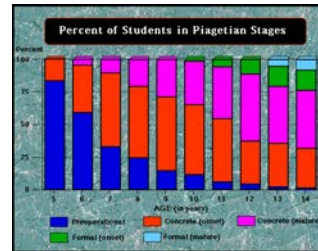


Piaget and Plato's Cave



Society and Formal Conception

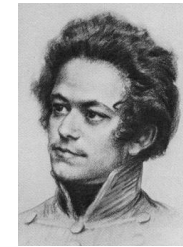
- The majority of people attain a mature level of concrete operational thinking.
- Only a small portion arrive at a mature level of formal conceptualization.
- “Nature” targets a 16 year old reading level.



Folly of Freud, Marx and Einstein



It's not all about me



It's not society's fault



It's not all relative

Liberal Education

We cannot live physically on food digested by others. How then should we do it mentally?

What do we know?

How do we know it?

Critical Systems Analysis
Deductive Logical Process
Constructive Composition

Models as Abstraction of Human Experience

(Profumo Caveat – Beware the danger of playing with models)

The fruit of liberal education is not learning, but the capacity and desire to learn, not knowledge, but power. – **Charles W. Eliot**